

CLAIMS

1. A method, comprising:
permeating a pH-altering agent into a predetermined reaction site having a
volume of less than about 1 ml.
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2. A method as in claim 1, wherein the predetermined reaction site is able to maintain
at least one living cell.
3. A method as in claim 1, wherein the pH-altering agent comprises ammonia.
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4. A method as in claim 1, wherein the pH-altering agent comprises acetic acid.
5. A method as in claim 1, wherein the pH-altering agent is a gas.
- 15 6. A method as in claim 1, wherein the pH-altering agent comprises CO₂.
7. A method as in claim 1, wherein the pH-altering agent, when contacted with water,
reacts to produce an acid.
- 20 8. A method as in claim 7, wherein the pH-altering agent, when contacted with water,
reacts to produce carbonic acid.
9. A method as in claim 1, wherein the pH-altering agent, when contacted with water,
reacts to produce a base.
- 25 10. A method as in claim 1, wherein the pH-altering agent is a liquid.
11. A method as in claim 1, wherein the permeating step comprises permeating the pH-
altering agent across a surface defining a portion of a boundary of the predetermined
30 reaction site.

12. A method as in claim 11, wherein the diffusing step comprises permeating at least some of the pH-altering agent across the surface in a time of less than about 10 minutes.
- 5 13. A method as in claim 11, wherein the diffusing step comprises permeating at least some of the pH-altering agent across the surface in a time of less than about 5 minutes.
- 10 14. A method as in claim 11, wherein the diffusing step comprises permeating at least some of the pH-altering agent across the surface in a time of less than about 3 minutes.
- 15 15. A method, comprising:
providing a chip comprising a predetermined reaction site having a volume
of less than about 1 ml;
generating an acid or a base proximate the predetermined reaction site; and
contacting the acid or base with a substance within the predetermined
reaction site to substantially alter the pH of the substance.
- 20 16. A method as in claim 15, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
17. A method as in claim 15, wherein the contacting step comprises altering the pH by at least 0.3 pH units.
- 25 18. A method as in claim 15, wherein the contacting step comprises altering the pH by at least 0.5 pH units.
19. A method as in claim 15, wherein the contacting step comprises altering the pH by at least 1 pH unit.
- 30 20. A method as in claim 15, wherein the acid or base comprises ammonia.

21. A method as in claim 15, wherein the acid or base comprises acetic acid.
22. A method as in claim 15, wherein the acid or base comprises carbonic acid.
- 5 23. A method as in claim 15, wherein the generating step comprises chemically reacting a precursor to produce the acid or base.
24. A method as in claim 23, wherein the precursor comprises a salt.
- 10 25. A method as in claim 23, wherein the generating step comprises thermally decomposing the precursor.
26. A method as in claim 23, wherein the generating step comprises exposing the precursor to energy.
- 15 27. A method as in claim 26, wherein the energy comprises electromagnetic energy.
28. A method as in claim 26, wherein the energy comprises electrical energy.
- 20 29. A method, comprising:
providing a chip defining at least one compartment, the chip further comprising a predetermined reaction site having a volume of less than about 1 ml;
and
25 permeabilizing a component positioned between the predetermined reaction site and the at least one compartment.
30. A method as in claim 29, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
- 30 31. A method as in claim 29, wherein the permeabilizing step comprises exposing the surface to an agent that increases the permeability of the component.

32. A method as in claim 29, wherein the permeabilizing step comprises increasing the temperature of the component.
- 5 33. A method as in claim 29, further comprising allowing an agent to move across the component.
34. A method as in claim 29, further comprising allowing an agent to permeate across the component.
- 10 35. A method as in claim 29, further comprising allowing an agent to move from the at least one compartment to the predetermined reaction site.
- 15 36. A method as in claim 29, wherein the permeabilizing step comprises increasing the permeability of the component to an agent by at least about 2 orders of magnitude.
37. A method as in claim 29, wherein the permeabilizing step comprises increasing the permeability of the component to an agent by at least about 3 orders of magnitude.
- 20 38. A method as in claim 29, wherein the permeabilizing step comprises increasing the permeability of the component to an agent by at least about 4 orders of magnitude.
39. A method as in claim 29, wherein the permeabilizing step comprises decomposing at least a portion of the component.
- 25 40. A method as in claim 39, wherein the decomposing step comprises exposing the surface to an agent that decomposes at least a portion of the component.
41. An apparatus, comprising:
- 30 a chip comprising a predetermined reaction site having a volume of less than about 1 ml; and

a component separating the predetermined reaction site from a source of a non-pH-neutral composition.

- 5 42. An apparatus as in claim 41, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
43. An apparatus as in claim 41, wherein the component is permeable to a gas.
- 10 44. An apparatus as in claim 41, wherein the component is permeable to CO₂.
45. An apparatus as in claim 41, wherein the component is permeable to a liquid.
- 15 46. An apparatus as in claim 41, wherein the predetermined reaction site has a volume of less than about 500 microliters.
47. An apparatus as in claim 41, wherein the predetermined reaction site has a volume of less than about 100 microliters.
- 20 48. An apparatus as in claim 41, wherein the predetermined reaction site has a volume of less than about 10 microliters.
49. An apparatus as in claim 41, wherein the predetermined reaction site has a volume of less than about 1 microliter.
- 25 50. An apparatus as in claim 41, wherein the predetermined reaction site has a maximum dimension of less than about 1 cm.
51. An apparatus as in claim 41, wherein the predetermined reaction site has a maximum dimension of less than about 1 mm.
- 30 52. An apparatus as in claim 41, wherein the predetermined reaction site has a maximum dimension of less than about 100 micrometers.

53. An apparatus as in claim 41, wherein the predetermined reaction site has a maximum dimension of less than about 10 micrometers.
- 5 54. An apparatus as in claim 41, wherein at least one surface of the predetermined reaction site comprises a polymer.
55. An apparatus as in claim 41, wherein the component is acid-permeable.
- 10 56. An apparatus as in claim 41, wherein the component is alkaline-permeable.
57. An apparatus as in claim 41, wherein the component comprises a polymer.
58. An apparatus as in claim 41, wherein the component comprises
15 polydimethylsiloxane.
59. An apparatus as in claim 41, wherein the component comprises a silicone.
60. An apparatus as in claim 41, wherein the component has a permeability of at least
20 about $590 \text{ cm}^3_{\text{STP}} \text{ cm/s cm}^2 \text{ cmHg}$ to ammonia.
61. An apparatus as in claim 41, wherein the component has a permeability of at least
about $500 \text{ cm}^3_{\text{STP}} \text{ cm/s cm}^2 \text{ cmHg}$ to acetic acid
- 25 62. An apparatus, comprising:
a chip comprising a predetermined reaction site having a volume of less than
about 1 ml; and
a precursor able to react to form a gaseous agent able to substantially alter
the pH of a substance within the predetermined reaction site,
30 wherein the chip is arranged to allow gaseous non-liquid transport of the
agent to the predetermined reaction site.

63. An apparatus as in claim 62, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
64. An apparatus as in claim 62, wherein the precursor comprises a source of acid gas.
- 5 65. An apparatus as in claim 62, wherein the precursor comprises a source of alkaline gas.
66. An apparatus as in claim 62, wherein the precursor comprises CO₂.
- 10 67. An apparatus as in claim 62, wherein the precursor comprises a salt.
68. An apparatus as in claim 62, wherein the source comprises a radiation-absorbing material.
- 15 69. An apparatus as in claim 62, wherein the source is activatable upon absorption of energy.
- 20 70. An apparatus as in claim 69, wherein the source is activatable upon absorption of electromagnetic radiation.
71. An apparatus as in claim 62, wherein the source is activatable at a temperature of at least about 200 °C.
- 25 72. An apparatus as in claim 62, wherein the source is activatable at a temperature of at least about 300 °C.
73. An apparatus as in claim 62, wherein the source is activatable at a temperature of at least about 500 °C.
- 30 74. An apparatus, comprising:
a chip comprising a predetermined reaction site having a volume of less than

about 1 ml; and

a pH-altering agent dispensing unit integrally connected to the chip in fluid communication with the predetermined reaction site.

- 5 75. An apparatus as in claim 74, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
76. An apparatus as in claim 74, wherein the acid or base dispensing unit is able to generate the acid or base.
- 10 77. An apparatus as in claim 76, wherein the acid or base dispensing unit is connectable to a source of a precursor of the acid or base.
78. An apparatus as in claim 77, wherein the source of the precursor comprises a source of CO₂.
- 15 79. An apparatus as in claim 74, wherein the acid or base dispensing unit is connectable to a source of acid or base.
- 20 80. An apparatus, comprising:
 a chip comprising a predetermined reaction site having a volume of less than about 1 ml; and
 a source of gas integrally connected to the chip.
- 25 81. An apparatus as in claim 80, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
82. An apparatus as in claim 80, wherein the source of gas comprises a precursor compound.
- 30 83. An apparatus as in claim 80, wherein the source of gas comprises a salt.

84. An apparatus as in claim 80, wherein the source of gas is able to produce gas upon application of energy thereto.
85. An apparatus as in claim 84, wherein the energy comprises electromagnetic energy.
- 5 86. An apparatus as in claim 80, wherein the source of gas comprises at least one sealed compartment.
87. An apparatus as in claim 80, wherein the source of gas is not in fluid communication with the predetermined reaction site.
- 10 88. An apparatus as in claim 80, wherein the gas is a non-pH-neutral gas.
89. An apparatus as in claim 80, wherein the gas is an acidic gas.
- 15 90. An apparatus as in claim 80, wherein the gas is an alkaline gas.
91. An apparatus as in claim 80, wherein the gas comprises CO₂.
- 20 92. An apparatus, comprising:
a chip comprising a predetermined reaction site having a volume of less than about 1 ml; and
a laser waveguide in optical communication with a surface defining the predetermined reaction site.
- 25 93. An apparatus as in claim 92, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.
94. A method, comprising:
30 producing a gas in a chip comprising a predetermined reaction site having a volume of less than about 1 ml by directing a laser at at least a portion of the chip.

95. A method as in claim 94, wherein the chip is constructed and arranged to maintain at least one living cell at the predetermined reaction site.